

REMARKS

Claims 1-10, 12 and 13 are pending in this application.

I. Claim Rejection Under 35 U.S.C. § 103

The Examiner rejects claims 1-10, 12 and 13 under 35 U.S.C. § 103(a) as being unpatentable over Kita et al. (US 6,307,052) (“Kita”) in view of Lehmuusaari et al. (US 5,795,913) (“Lehmuusaari”). Applicant respectfully traverses the rejection.

The preparation and eye drops of claims 1, 10 and 13 require a water-soluble metal chloride in a light-stabilizing effective amount of **0.2 w/v% or more**.

In the final Office Action, the Examiner admits that while Kita teaches a medical composition comprising bepotastine, the reference does not specifically teach how the composition is formulated, and does not specifically teach a water-soluble metal chloride in a light-stabilizing effective amount of 0.2 w/v% or more (see page 3, fourth paragraph).

In the Advisory Action, the Examiner states, “Lehmussari teaches that the purpose of the salt is to reduce the viscosity, since doing so is favorable both from the view point of efficacy of the product in the target site, and of ease of application; additionally, if no salts are added, a formulation with an unacceptably high viscosity is obtained (col. 3, lines 38-50). Therefore, one skilled in the art would be motivated to manipulate the amount of the salt from within the range taught by Lehmussari, including greater than 0.2%, in order to optimize the efficacy and ease of application of the resultant composition” (see lines 4-10).

The mere fact that references may be combined does not render the resultant combination obvious **unless the results would have been predictable to one of ordinary skill in the art** (see MPEP 2143.01.III). The combination of Kita and Lehmussari would not have led to predictable results.

A person of ordinary skill in the art would not have been motivated to select a metal chloride from all of the salts and buffers disclosed in Lehmussari and then manipulate the amount of the salt and/or buffer to arrive at 0.2 w/v% from the broad range of 0.01-1.5%.

The objective of Lehmuusaari is to reduce the viscosity of a composition comprising an ophthalmologically active agent containing basic groups and a viscosity enhancer (a hydrophilic polymer containing acidic groups) by the addition of a salt and/or a buffer (see col. 3, lines 25-46).

On the other hand, the objective of the present application is to **light-stabilize** a bepotastine aqueous liquid preparation by the addition of a metal chloride. These effects are completely different, and the constitutional requirements are also different. It is clear that the objective of adding a salt is different between the present application the Lehmuusaari.

Moreover, Lehmuusaari teaches, “For some purposes, for example for **appearance** and storage purposes, **the use of a buffering salt is preferred to the use of e.g. sodium or potassium chloride** as the viscosity reducing agent” (see col. 3, lines 55-58, emphasis added). In view of this description, a person of ordinary skill in the art would expect that the appearance is stable when a bepotastine aqueous liquid preparation contains a buffer of phosphate, borate or the like, rather than sodium chloride or potassium chloride.

In the examples of the present application, the changes in the appearance of a bepotastine aqueous liquid preparation were observed after light irradiation. The appearance of a bepotastine aqueous liquid preparation containing a metal chloride was **more stable** than a preparation containing a buffer. The results are **completely opposite and unexpected** from the teaching of Lehmuusaari that for appearance and storage purposes, the use of a buffering salt is preferred to the use of sodium or potassium chloride as the viscosity reducing agent.

Specifically, Formulations 3-7 of the present application contain 0.2% or more of a metal chloride, and these formulations did not immediately change after preparation. On the other hand, Formulations 8 and 9, which do not contain a metal chloride but do contain a buffer (boric acid), changed into black green and a precipitate was observed (see page 9, lines 5-13 of the specification). Moreover, Formulations 13-17, which do not contain a metal chloride but do contain a buffer (phosphate) also changed into black green, blue or yellow brown, and Formulations 13-16 produced a precipitate in addition to a change in color (see page 11, lines 7-23 of the specification).

These results demonstrate that a bepotastine aqueous liquid preparation is more stable when it contains sodium chloride rather than a buffer. This is completely opposite and unexpected from Lehmuusaari, which teaches that for **appearance** and storage purposes, **the use of a buffering salt is preferred to the use of sodium or potassium chloride** as the viscosity reducing agent.

The claimed composition demonstrates prominent and unexpected light-stability without a change of appearance caused by light irradiation. This is completely inconsistent with the teachings of Lehmuusaari. Therefore, a person of ordinary skill in the art would not have been motivated to select metal chloride from all of the salts and buffers disclosed in Lehmuusaari and then manipulate the amount of the salt and/or buffer to arrive at 0.2 w/v% from the broad range of 0.01-1.5 w/v % disclosed in the reference.

Accordingly, the prominent effect of the claimed invention would not have been predictable to one of ordinary skill in the art from the teachings of Lehmuusaari, and thus the combination of Kita and Lehmuusaari would not have led to predictable results.

Therefore, claims 1, 10 and 13 would not have been obvious over the references.

Claims 2-9 and 12 depend directly or indirectly from claim 1, and thus also would not have been obvious over the references.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

II. Conclusion

For these reasons, Applicant takes the position that the presently claimed invention is clearly patentable over the applied references.

Therefore, in view of the foregoing remarks, it is submitted that the rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

Masayo HIGASHIYAMA

By /Andrew B. Freistein/
Freistein/

Digitally signed by /Andrew B. Freistein/
DN: cn=/Andrew B. Freistein/, o=WLP,
ou=WLP, email=afreistein@wenderoth.
com, c=US
Date: 2011.05.19 12:59:16 -04'00'

Andrew B. Freistein
Registration No. 52,917
Attorney for Applicant

ABF/emj
Washington, D.C. 20005-1503
Telephone (202) 721-8200
Facsimile (202) 721-8250
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